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10/566,445	08/21/2006	Sergio Bodini	105515-4000	5159

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EXAMINER	
SINGH, SATYENDRA K	
ART UNIT	**PAPER NUMBER**
1657	

NOTIFICATION DATE	DELIVERY MODE
04/29/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/566,445	BODINI ET AL.	
	Examiner	Art Unit	
	SATYENDRA K. SINGH	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 January 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-48* is/are pending in the application.

4a) Of the above claim(s) *33-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/31/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response and amendments to claims filed on 01/26/2009 is duly acknowledged.

Newly presented claims 25-48 are pending in this application. Claims 1-24 are canceled and 33-48 are withdrawn by applicant's current amendments.

Claims 25-32 (corresponding to original group I) are elected and examined on their merits in this office action.

Election/Restrictions

Applicant's election of **group I** (newly presented claims 25-32; directed to **an induction solution for rapid detection of coliform cells**; corresponding to the original claims 1-8, group I) in the reply filed on 01/26/2009 is acknowledged. Because applicants did not distinctly and specifically point out the supposed errors in the restriction requirement, and did not specify whether the election was made with or without traverse, the election has been treated as an **election without traverse** (MPEP § 818.03(a)).

The restriction/election as set forth in the previous office action is still deemed proper, and is made FINAL.

Applicants are advised that the dependence of newly presented claim 42 (directed to an analysis kit) on instant claim 33 (the invention directed to a method of use) has been taken as a typographical error, and is presumed (in view of original claim 9 that depended from claim 1) to be depended from the product of group I (i.e. new claim 25 directed to the "induction solution"). Applicants are advised to amend the claims appropriately to reflect this fact.

Claim Rejections - 35 USC § 112- New Matter

The following is a quotation of the **first paragraph** of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 25-32 (newly presented) are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Newly presented claim 25 recites the limitation of "wherein said amino acid concentration is about 80 mM". Insertion of the limitation "wherein said amino acid concentration is **about 80 mM**" does not have proper support in the as-filed specification. The insertion of this limitation is **a new concept** because it neither has literal support in the as-filed specification by way of generic disclosure, nor are there specific examples of the newly limited genus which would show possession of the concept of the use of a mixture of amino acid(s) at "about 80 mM". The only exemplification on page 12, [0035] uses 0.27 mM of a mixture of all 20 natural amino acids in the "induction solution". In addition the generic disclosure on page 7, paragraph [0025] for the amount of amino acids states that "...*in general the use of the all natural 20 amino acids, promoters of the induction, is preferable but not necessary, at a concentration, preferably but not necessarily,* ***0.02mM each***...", which will make the total concentration for a mixture of all 20 natural amino acids to 20x0.02= 0.4 mM, not "about 80 mM" as currently amended. The disclosure suggests the concentration of certain amino acids "up to 80 mM" (see specification, page 7, [0025], Reagent A).

However, this is not sufficient support for the newly limited genus of amino acid concentration (for a mixture of 20 amino acids as claimed in claim 28, for example) of "about 80 mM" as recited in newly presented claim 25 (that requires said concentration to be "about 80 mM"; see also discussion below). This is a matter of written description, not a question of what one of skill in the art would or would not have known. The material within the four corners of the as-filed specification must lead to the generic concept. If it does not, the material is new matter. Declarations and new references cannot demonstrate possession of a concept after the fact. Thus, the limitation of "about 80 mM" is considered to be the insertion of **new matter** for the above reasons. Appropriate explanation/correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 25-32 (newly presented) are rejected under 35 U.S.C. 112, second paragraph, as being **indefinite** for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 25 recites the limitation of "wherein said amino acid concentration is at about 80 mM", which is ambiguous. It is unclear as to what exactly is encompassed by the limitation as presented, especially in light of the original disclosure filed by applicants (see instant disclosure, page 12, section "Mode for the Invention", last paragraph [0035], in particular), which recites the following:

"[0035] Enzyme induction

> 33 μl of sample were added to 2315 μl of filter-sterilized (0.45 μm) induction solution, at pH 7.2, comprising sodium hydrogen phosphate (Na2HPO4) 47.7 mM, potassium dihydrogen phosphate (KH2PO4) 22 mM, magnesium sulphate heptahydrate (MgSO4"7H20) 0.5 mM, 80 μg of natural amino acids (alanine A, cysteine C, aspartic acid D, glutamic acid E, phenylalanine F, glycine G, histidine H, isoleucine I, lysine K, leucine L, methionine M, asparagine N, proline P, glutamine Q, arginine R, serine S, threonine T, valine V, tryptophan W, tyrosine Y, **4 μg each**), 250 μg of sodium dodecyl sulphate and 125 μg of β-galactosidase inducer isopropyl-β-D-thiogalactopyranoside; the mixture was then incubated at 37°C for 75 minutes."

First, it is unclear if the recitation "said amino acid concentration" refers to the concentration for "one amino acid" or to "a mixture of amino acids" to be at "about 80 mM". Second, the guidance provided by applicants in the section "Mode of Invention" regarding the concentration used for the mixture of 20 natural amino acids translates to 3.4557 mg per liter (i.e. total 80 micrograms in 2.315 ml of induction solution, which comes to about 0.27 mM; taking 130.0 g/mol as an average molecular weight of all 20 natural amino acids), which is no where closer to the actual claimed value "about 80 mM". In addition the generic disclosure on page 7, paragraph [0025] for the amount of amino acids states that "...*in general the use of the all natural 20 amino acids, promoters of the induction, is preferable but not necessary, at a concentration, preferably but not necessarily,* ***0.02mM each***...", which will make the total concentration for a mixture of all 20 natural amino acids to 20x0.02= 0.4 mM, not "about 80 mM" as currently claimed. Therefore, an artisan of ordinary skill in the art would not understand as to what exactly is being encompassed by the limitations as currently claimed by applicants. Appropriate explanation/correction is required.

Since, claims 26-32 directly or indirectly depend from claim 25, they are also rejected as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

For examination and prior art purposes herein, the instant claims are being interpreted **as currently written** (i.e. "said amino acid concentration is at **about 80 mM**").

2. Claim 32 recites the limitation "**said selective agent**" in line 1. There is insufficient antecedent basis for this limitation in the broader claim 25. Applicants are advised to amend claim 32 such that it depends from claim 31 in view of the subject matter being claimed (i.e. a selective agent). Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names **joint inventors**. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1. Claims 25-32 (as currently presented) are rejected under 35 U.S.C. 103(a) as being unpatentable over Nelis (US 5,861,270; issued on January 19, 1999; IDS) in view of Kuroda (PNAS, 1999; [U]).

Claims are directed to "an induction solution" for rapid detection of coliform cells, capable of inducing the expression of inducible enzymes, beta-glucuronidase and beta-galactosidase, in the absence of cell growth, comprising: at least one amino acid (does not specifically require purified amino acid) or a mixture of amino acids, being at a concentration that does not allow a detectable coliform cell growth within a time period of between 0-120 minutes when the coliform cells come in contact with said at least one amino acid or said mixture of amino acids and wherein said amino acid concentration is at about 80 mM; a buffer system; a bivalent ion; and an enzymatic inducer consisting of isopropyl-beta-D-thiogalactopyranoside (IPTG) and/or methyl-beta-D-glucuronide (see instant claims 26-28); wherein said bivalent ion is Mg++ and said Mg++ is used at a concentration of about 0.05 mM; wherein said isopropyl-beta-D- thiogalactopyranoside is used at a concentration of about 0.2 mM and/or said methyl-beta-D- glucuronide is used at a concentration of about 2 mM; and wherein said induction solution further comprises a selective agent that acts as a membrane permeabilizer such as sodium dodecyl sulphate (SDS).

Nelis (IDS) discloses an induction solution for rapid detection of coliform cells, capable of inducing the expression of inducible enzymes, beta-glucuronidase and beta-galactosidase, in the absence of growth of competing bacteria (see abstract, summary of the invention on column 2, column 4, and example 1 and 3, in particular), comprising: a protein hydrolysate such as tryptone and yeast extract, a buffer system such as monoammonium phosphate/dipotassium phosphate; a bivalent ion such as magnesium

in the form of magnesium sulfate and magnesium chloride; and an enzymatic inducer consisting of IPTG; and wherein said induction solution further comprises a selective agent that acts as a membrane permeabilizer such as sodium dodecyl sulphate (SDS; see summary of the invention and columns 8, 1st paragraph, and column 9, example 3, in particular); and wherein beta-glucuronidase inducer such as methyl-beta-D-glucuronide may be used in said induction solution (see column 5, 1st paragraph and claim 20, in particular). Nelis discloses the problem with the growth of other non-coliform bacteria that produce background luminescence, and wants to reduce detection time and the quenching of light emission due to growth of non-target bacteria (see summary of the invention, and column 3, in particular).

However, an induction solution comprising **at least one amino acid, or a mixture** of all 20 **amino acids** (claims 26-28; taken as purified amino acids supplemented to said solution) at a concentration of **about 80 mM** is not taught by the invention of Nelis.

Kuroda et al [U] disclose an induction solution (suitable for rapid detection of coliform cells, capable of inducing the expression of inducible enzymes, beta-glucuronidase and beta-galactosidase, in the absence of cell growth) comprising at least one amino acid or a mixture of amino acids (see Kuroda et al, page 14264, "Materials and Methods", section on "Nutritional Downshift"; figure 3 and 6, in particular), wherein said amino acid concentration is at about 10 micromolar to about 0.4 mM (uses supplementation of all 20 natural amino acids at 1.25, 10, and 50 mg/liter; see figure 6 and its legend, page 14267, left column, in particular); a buffer system such as MOPS, pH 7.2; a bivalent ion such as magnesium or calcium; and an enzymatic inducer consisting of isopropyl-beta-D-thiogalactopyranoside (IPTG) at a concentration

of 1 mM (see legend of figure 6 A and B). In addition, Kuroda et al demonstrates induction of beta-galactosidase (i.e. lacZ expression) by the nutritional downshift in the wild type *E. coli* (see page 14266, right column, last paragraph, in particular), and the fact that availability of free amino acids (supplemented in the MOPS minimal growth medium) is important for the enzyme production (i.e. beta-galactosidase) after the nutritional down shift (see page 14267, right column, 1st paragraph, in particular).

Thus, at the time the claimed invention was made, it would have been obvious to an artisan of ordinary skill in the microbial detection art to modify the induction solution of Nelis (see discussion above) such that it uses a defined medium supplemented with purified amino acid(s) or a combination thereof (as taught by Kuroda et al; instead of protein hydrolysates such as yeast extract and peptone; see Kuroda et al page 14264, section "nutritional downshift", in particular) in order to avoid high background due to non-coliform bacterial growth and thus higher background fluorescence resulting from growth on rich medium.

Since, Kuroda et al disclose the benefits of nutritional downshift in terms of the induction of beta-galactosidase by amino acid supplementation, one of the marker enzymes used in detection of coliforms by Nelis, one of ordinary skill in the art would have been motivated at the time of invention to make this modification/substitution in the induction solution of Nelis in order to obtain a better and sensitive induction solution as suggested by the combined teachings of the cited prior art references, with a reasonable expectation of success.

The limitations of molar concentrations of amino acids (that allows no detectable coliform cell growth within a time period of between 0-120 minutes), magnesium ions, and enzymatic inducers used in the induction solution would have been obvious to an artisan of ordinary skill in the microbial detection art at the time this invention was made because the cited prior art references of Nelis and Kuroda et al disclose various combinations of concentrations (see for amino acids supplementation of a defined medium, Kuroda et al, figure 6, legend, in particular; and for both Nelis and Kuroda et al for the amounts of bivalent ion such as magnesium, IPTG, etc.; see discussion above) that may be further varied by an artisan of ordinary skill depending upon the specific requirement of the detection system, and in order to obtain a highly sensitive assay for coliforms having lower background fluorescence, as desired by the disclosure of Nelis (see discussion of Nelis above). Since, the nutritional downshift is known to reduce growth of bacteria on a defined medium as explicitly disclosed by Kuroda et al, the use of amino acid supplementation to help induce lacZ expression (with the help of an enzymatic inducer such as IPTG) as an enzymatic marker in a rapid detection system for coliforms would have been obvious to an artisan at the time the claimed invention was made. The claimed subject matter fails to patentably distinguish over the state of the art as represented by the cited references.

Thus, the invention as a whole would have been *prima facie* obvious to a person of ordinary skill in the art at the time the claimed invention was made.

As per MPEP 2111.01, *during examination, the claims must be interpreted as broadly as their terms reasonably allow. In re American Academy of Science Tech Center, F.3d, 2004 WL 1067528 (Fed. Cir. May 13, 2004)(The USPTO uses a different standard for construing claims than that used by district courts; during examination the USPTO must give claims their broadest reasonable interpretation.). This means that the words of the claim must be given their plain meaning unless applicant has provided a clear definition in the specification. In re Zletz*, 893 F.2d 319, 321, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989).

As per MPEP 2144.06, *In order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents. In re Ruff, 256 F.2d 590, 118 USPQ 340 (CCPA 1958).*

As per MPEP 2144.05 [R3], II. OPTIMIZATION OF RANGES - A. Optimization Within Prior Art Conditions or Through Routine Experimentation: *Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).*

Conclusion

NO claims are allowed.

Applicants are advised that certain prior art rejections under 35 USC 102(b) have not been made **in view of the current claim amendments** (i.e. newly presented claim 25, in particular the limitation of "about 80 mM" in line 7) that are deemed to constitute "**new matter**" as discussed above (see 35 USC 112, first paragraph rejection *supra*), and may be relied upon in future depending upon further claim amendments during prosecution.

Pertinent Prior Art nor relied upon in Rejections:

1. Urabe et al. (US 6251661 B1; issued on 26 June 2001) Seamless capsule for synthesizing biopolymer for producing the same (see column 12-13, table for LM mixture, in particular).
2. Chang et al. (US 5,411,867; issued on May 2, 1995) Method for determination of E. coli in water (see abstract, example 3, lines 25-32, in particular).
3. Estes C. et al. Reagentless detection of microorganisms by intrinsic fluorescence, Biosensors and Bioelectronics, April 12, 2003, volume 18, pages 511-519.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SATYENDRA K. SINGH whose telephone number is (571)272-8790. The examiner can normally be reached on 9-5MF.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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